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(54) Title: PHARMACEUTICAL DISINFECTANTS COMPRISING USNIC AND ESSENTIAL OILS

(57) Abstract: The process relates to the pharmaceutical disinfective preparation on the basis of usnic acid sodium salt and medical plants (sage *Salvia officinalis* L., or fennel *Foeniculum vulgare* L., or thyme *Thymus Vulgaris* L., or peppermint *Mentha piperita* L.) or menthol, which is used as a common disinfective agent for external use in treatment of inflammation of the upper respiratory tract and oral cavity, caused by the action of pathogenic microorganisms. The invention presents the procedures for obtaining of the preparations in the form of: chewable tablets, tablets, gel, aerosol, as a base for deodorants, aromatic-antiseptic liquid for disinfection, in the form of wet napkin for intimate care, baby powder and other forms for mentioned purpose.

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PHARMACEUTICAL DISINFECTANTS COMPRISING USNIC ACID AND ESSENTIAL OILS

The field of technique

Suggested invention generally falls into the field of pharmaceutical preparations on the basis of usnic acid sodium salt and medical plants (sage *Salvia officinalis* L., fennel *Foeniculum vulgare* L., thyme *Thymus Vulgaris* L., or peppermint *Mentha piperita* L.) or menthol, which are used for disinfection and for the process for their obtaining.

Technical problem

Technical problem which is solved by this invention consists of a problem how to incorporate the active components, in this case usnic acid sodium salt (sodium salt obtained from usnic acid) and essential oils from the upper parts of medical plants (sage *Salvia officinalis* L., fennel *Foeniculum vulgare* L., thyme *Thymus Vulgaris* L., or peppermint *Mentha piperita* L.) or menthol, into suitable base, which is the best way to preserve their active properties, caused by synergistic effect of above mentioned active principles and to provide simple application for disinfection of mouth and throat.

Background of the invention

There are already known preparations for disinfection of mouth and throat, with incorporated active components containing additives (essential oils, extracts, tinctures,...), or medicinal parts of herbal drugs (sage, fennel, thyme, or peppermint).

Sage – *Salvia officinalis* L. is a carminative, spasmolytic, antiseptic, astringent and diarrhoic. It neutralizes influenza virus and enhances leukocytes function (phagocytic activity). Leaf is used, and it is an antiphlogistic, stomachic, antisudorific, spice, especially its essential oil as an antiseptic. Sage leaf is used as a gargle for inflammation of the mouth and throat, digestive complaints, flatulence, inflammation of the intestinal

mucosa, in diarrhoea, as an antisudorific (antihydrotic), against night sweats in tuberculosis patients, but also against excessive sweat formation of psychosomatic origin. In folk medicine, because of an inhibiting effect on the secretion of milk, garden sage is also used to aid the cessation of lactation; it is also said to have mild hypotensive and emmenagogic effects. The ancient physicians were using sage very much against chronic lung illnesses and as a rinse for inflammation and catarrh of the mouth and troath. Traditionally, it is used against dyspepsia, pharyngitis, uvultis, stomatitis, gingivitis, glossitis, *hyperhydrosis* and *galactorrhoea*. Spanish oil does not contain thujone, instead, the share of cineole is greater. The oil *Salvia triloba* contains just a small amount of thujone, and because of its high content of cineole, it reminds of eucalyptus oil, by the odour. Diterpenoid bitter substances Carnosol (Picrosalvin) which is additionally contained in Dalmatian and Greek sage, are missing in Spanish sage. Carnosol and ringlike open form, which is not bitter, carnosic acid, cannot be obtained by steam distillation, but by extraction of the drug with petrol. Sage also contains triterpenoid acids (Ursol- and Oleanol-acid), flavonoids and tannins. Salvigenin, 5-hydroxy-6,7,4-trimetoxy-flavone is characteristic for *Salvia triloba*, and is used to detect forgery.

Table 1. Contents of active components in essential oil of different kinds of sage

Kind of sage	Essential oil			Bitter substances	
	□,□,□- thujone	Cineole	Camph or	Borneol	Carnosol
Dalmatian sage	40-60%	12-15%	7-8%	5-7%	ca. 0,35%
Spanish sage	-	30-35%	ca. 30%	ca. 8%	-
Greek sage	ca. 5%	60-70%		ca. 0,35%	ca. 0,20%

Fennel fruit – *Foeniculum vulgare* L. contains 4-6,5% of essential oil obtained by distillation. The essential oil contains approximately 60% of anethole, 12% of fenchone, methylcavicol, □-pinene, canphene, etc. There is fatty oil, comprising 60% of petroselenic acid, 22% of oleic acid, 14% of linolenic acid, and 4% of palmitic acid, in the fruit. The drug contains quercetin, flavons and insufficient amount of essential oil.

The fruits are gathered in phase of puberty. In folk medicine, it is used as a galactagogue for lactating women, and externally as an eye lotion (decoction) and in functional visual disorders. Fennel is also used for appetite enhancement. Fennel fruit possesses a carminative, aromatic, antiinflammatory, antimicrobial and diuretic action. Recently, fennel is more often used as an expectorant (secretolytic, secretomotoric, antiseptic), spasmolytic, and carminative. Fennel fruit and preparations thereof are used in disturbed intestinaldriving functions, in spasmic colitis, and meteorism. The fruits of fennel – *Fructus Foeniculi* are used, and they contain 2-6% of essential oil and 9-12% of fatty oil; in addition, essential oil – *Oleum Foeniculi*, colourless to weakly yellowish liquid, comprising fenchone and anethole as main constituents. Fennel is a mild expectorant, mostly for children. It is considered to counteracts cramps, even to possesses mild narcotic action. Fennel is an excellent corrigent of taste in carminative tea mixtures. Fennel tea is used against dyspepsia and diarrhea in infants. It does not only bring liquid into organism, but, also reduces intestinal meteorism and spasm, using its carminative effect. Pure fennel essential oil reinforces inflammation, and has an irritant action on the intestinal musculature, and must not be used for infants or young children because of the danger of laryngeal spasm, *dyspnoea*, and excitatory states.

Thyme – *Thymus Vulgaris L.* is used as a carminative, antispasmodic, antitussive, expectorant, secretomotoric, bactericid, anthelmintic, and astringent. Traditionally, it is used against dyspepsia, chronic gastritis, asthma, diarrhea in children, enuresis in children, laryngitis, tonsillitis, and especially against influenza and bronchitis. Externally, thyme is used as a hyperaemic, antibacterial, and also deodorizing agent in inflammation of the mouth and throat (as a gargle) and as a rubefacient, additive and *pot-pourri*. In folk medicine, because of its spasmolytic action, it is an important stomachic and carminative, and it is also used as a diuretic, urinary disinfectant, and vermifuge. Thyme is also employed as a spice and in making liqueurs. 1.0-2.5% essential oil contains mainly the isomeric monoterpenes thymol (30-70%) and carvacrol (3-15%), a small portion of the phenols in the drug is present as glucoside or galactoside. In the essential oil, there are other monoterpenes such as p-cymene, α -terpinene, limonene, etc. The composition of the oil depends to a large extent on the origin of and time of harvesting of the drug, the α -terpinene and thymol contents being lower at the end of the vegetative cycle. Both plant

sources afford an oil of similar composition, though there are differences in the content of thymol methyl ester: in *Thymus Vulgaris* it is 1.4-2.5% and in *Thymus Zygis* only 0.3% of the oil; the monoterpenes accumulated primarily in the peltate glandular trichomes. *Thymus Vulgaris* subsp. *aestivus* from Spain, produces oil characterized mainly by the occurrence of 1,8-cineole (22%), geranoil (17%), and geranyl acetate (20%). The drug also has tannins, flavonoids, and triterpenes. The main constituents of the oil are with 40-50% of thymol (2-isopropyl-5-methyl-1-phenol) and isomeric carvacrol. Quantitative ratio between the two phenols depends on species, origin, and growth conditions. The oil from *Thymus zygis* instead of thymol, contains for example almost only carvacrol. The differences between oils containing thymol, that is carvacrol, can be determined by crystallization test. The supplemental constituents of terpene: p-cimol, thymolmonomethylether, linalol, borneol, geranyol and terpene-KW (\square -pinene, p-cimene).

The main pharmacological characteristic of thyme is connected with the essential oil (thymol and carvacrol) and favonoids. The thyme oil has hypotensive and respiratory stimulating effect on rabbits, administered orally or intramuscularly and on cats, administered by intravenous injection; it reinforces rhythmical cardiac contractions in rabbits. Crystal thymol is obtained from the thyme oil, from *Trachyspermum ammi* (L) *sprague*, *Ocimum gratissium* L., *Monarda punctata* L. and *Monarda didyma* L. It is easily attainable by dehydration of piperitone. Racemic menthol is obtained from thymol by hydration. Thyme oil is secreted at inner line mostly into lung alveoli and thus through lungs, it is in effect, concentrated to the location of the disorder. Spasmolytic effect at bronchial spasm is a characteristic of thyme, and therefore it became a whooping cough remedy for children and adults suffering from bronchitis with convulsive character of cough. Patients with emphysema and asthma appreciate spasmolytic property of thyme, although it is used only as an auxiliary remedy in long therapy. Scope of its activity is very wide. What is mint for stomach and intestines, thyme is for trachea and bronchi.

Peppermint (*Mentha piperita* L.) contains up to 4% of essential oil containing minimum of 48% of menthol, menthone, menthofuran and other monoterpenes. The drug also contains up to 12% of tannins, flavonoids, triterpenes. Peppermint is a spasmolytic, carminative, diaforetic, local antiseptic, and virustatic.

Available patent and non-patent literature does not offer any similar, or any process at all, for obtaining of a pharmaceutical preparation on the basis of medical plants (sage *Salvia officinalis* L., fennel, thyme, or peppermint *Mentha piperita* L.) or menthol, and usnic acid sodium salt, which is used for disinfection of mouth and throat.

Description of technical problem solution with examples

Usnic acid sodium salt and essential oils of medical plants (fennel *Foeniculum vulgare* L., or sage *Salvia officinalis* L., or thyme *Thymus Vulgaris* L or peppermint *Mentha piperita* L.) and menthol are strong antimicrobial and antifungal agents. The preparation obtained according to the invention comprising these active principles, showing mutual synergistic action, provides its effective use as a disinfectant for upper respiratory tract.

The essential oils built in the preparation according to the invention, show exceptionally high microbiological activity, due to the presence of certain active components. Sage *Salvia officinalis* L. is used for external application in the form of a gargle or rinse, using antiseptic, fungicidal and antiphlogistic effect of the oil, for treatment of inflammation of oral cavity and pharynx. Applied internally, it inhibits secretion of saliva and sweat. Since thujone has toxic properties, sage preparations must not be given in unfoundedly high doses and for a long period. Sage oils contain: thujone, 1,8-cineole, p-cimen and camphor, thymol and carvacrol. It also contains folic acids – caffeic acid, chlorogenic acid, ellagic acid, ferulic acid, gallic acid, rosmarinic acid, tannins (3-8%). Parallel essential oil *Salvia officinalis* is produced from different species of *Salvia*, with reduced total ketones and high content of total alcohol. Thyme *Thymus Vulgaris* L. essential oil is used internally as an expectorant and bronchospasmolytic, for treatment of acute and chronic bronchitis, cough, catarrh of respiratory tract, secretion, it causes enhanced movement of bronchial fibers. It is the cause of reflex action on stomach, and on the other side, is direct action on bronchial mucous membrane, since the essential oil can be partly secreted through lungs. Antiseptic and bactericidal action of thymol is also outstanding, and it is 25 times stronger than phenol, but it is considerably

less toxic than phenol, and it is also a strong fungicid. Thyme contains: thymol, carvacrol. The content of 0,8-2,6% essential oil is represented by phenols, which are the main ingredients (20-80%), especially thymol and carvacrol, taking p-cimen and α -terpinen (monoterpenes), linalol, α -terpienol and thujon-4-ol (alcohol) into account. It also contains: flavonoids, caffeic acid, oleic acid, ursolic acid, saponines, tannins. **Fennel** *Foeniculum vulgare* L. is used in preparations for treatment of bronchitis as a disinfectant, antiinflammatory agent and expectorant. It contains fenchone, methylcavicol, α -pinene, canphene. Those species of fennel with high content of essential oil are also characterized by high content of fenchone. Other compounds are: Methylcavicol (Esdragol), anisaldehyde, foeniculin, terpineol. Content of essential oil is 4%: **Peppermint** *Mentha piperita* L. contains: menthol, menthone, menthofuran and other monoterpenes, and their action is enhanced by presence of usnic acid sodium salt, which determines antibacterial effect of the preparation on: *Staphylococcus aureus*, *Echerichia coli*, *Salmonella sp.*, *Bacillus subtilis*, *Candida*. Synergistic action of some active components of the mixture containing of usnic acid sodium salt and essential oils (fennel, or sage, or thyme, or peppermint) or menthol – shows unexpected improvement in action on pathogenic microorganisms. Such combinations are new, and they are not comprised by the prior art, as well as the effects of the action for disinfection of the mouth and throat.

This pharmaceutical disinfective preparation on the basis of usnic acid sodium salt and medical plants (sage, fennel, thyme, or peppermint) or menthol, is used as a general disinfectant for external use and for treatment of inflammation of uper respiratory tract and oral cavity, caused by action of pathogenic microorganisms. The invention presents obtaining of the preparation in the form of: chewable tablets, tablets, gel, aerosol, as a base for deodorants, aromatic-antiseptic liquid for disinfection, in the form of wet napkin for intimate care, baby powder and other forms for mentioned purpose. The procedure for obtaining of this preparation, according to the invention, is reliable because the active components, in this case usnic acid sodium salt and essential oils preserve their natural properties, because of simplicity of the procedure for obtaining, their original antimicrobial action is neither reduced, nor lost. The advantage of the invention is in choice of active effect (usnic acid sodium salt and essential oils: fennel, or sage, or thyme,

or peppermint) or menthol, in simplicity of the process for obtaining, as well as in simple application of the finished form of the preparation. The process used usnic acid sodium salt, obtained by a certain process from lichen *Usnea barbata* L. Wigg. This substance possesses strong antibacterial activity, particularly in oral cavity and upper respiratory tract. It is a surface antibiotic, of natural origin, which selectively inhibits carriers of an infection, not damaging healthy microflora of the mucous membrane. Peppermint essential oil contains approximately 40-80% of menthol, which is among other components of its composition one of the carriers of antimicrobial activity and aroma of the oil. Its incorporation in the preparation, according to the invention, provides a successful replacement of menthol by peppermint essential oil, not reducing the effect of the finished form of the preparation.

Suggested invention relates to the procedure for obtaining of pharmaceutical disinfective preparation in the form of **chewable tablets**, in fact, tablets for suckling, that is, solid dose forms, intended for local application of active medical substance to mucous membrane of the mouth and throat. They are mainly produced by compressing, that is contracting, a mixture of active components and auxiliary substances.

Chewable tablets contain 0,001-0,020% of usnic acid sodium salt and essential oils: 0,05-0,20% of fennel oil, or 0,20-0,30% of sage oil, or 0,005-0,020% of thyme oil, or 0,05-0,09% of peppermint oil, or 0,03-0,08% of menthol. The procedure starts when a certain quantity of glucose is weighted into the vessel of the apparatus for preparation of a granulate. A granulating agent solution is prepared separately, by weighting a certain quantity of water into a certain vessel, heating it to 35-80°C, adding usnic acid sodium salt, certain quantity of colour and binder. Granulation of glucose is carried out with the solution prepared in this way, dispersing the solution. When inserting of the solution is over, the granulate is drying to humidity of 5-3%. Unifying of the granulate is carried out by screening through 0,5-2 mm mesh. To the cooled granulate, essential oil (fennel, sage, thyme, or peppermint) solution is added, using sprayer for inserting. The granulate is dried to humidity which provides good tableting (max. 22%). The dried granulate is inserted into a certain vessel for homogenization, and a certain quantity of sliding agent,

such as magnesium stearate, is added. The granulate prepared in such way is transferred to the tableting machine, and forming of oribletes is carried out.

The suggested invention presents the process for obtaining of pharmaceutical disinfective preparation in the form of gel, containing at least two components: the solid and the liquid ones, and also possesses the characteristics of both solids and liquids. The solid component of the gel must be colloidal and liophilic with partially solvated and usually asymmetrical particles, homogenously dispersed in a liquid medium. The liquid phase is partially bound and it fills hollows inside the spacious grid (it is immobilized).

Gel, containing 0,01-0,06% of usnic acid sodium salt and 0,05-0,40% of essential oils: fennel, or sage, or thyme, or peppermint, or menthol. The procedure consists of weighting of certain quantity of water into the vessel of the apparatus for preparation of gel, adding of usnic acid sodium salt to the water, and stirring to dissolving. Then, a certain quantity of carboxypolymethylene is added, the mixture is stirred to homogenization and left to become swollen, for 7-21 hours. To the gel base, a neutralizing agent is added slowly, with stirring, for example, sodium hydroxid solution. In a certain quantity of ethanol, dissolve the essential oil of fennel, that is sage, that is thyme, that is peppermint, that is menthol. This solution is gradually, with stirring added to the gel-mass to homogenization. After that, a certain quantity of colour solution is added.

The invention also presents the procedure for obtaining of a pharmaceutical disinfective preparation in the form of aerosol, which represents a suspension of liquid phase in pressure gas. As a pressure gas chlorinated or fluorized carbonhydrates (fluorotrichlormethan, difluorodichloromethan or tetrafluorodichlor). The active medical substance can have the form of solution, emulsion, powder, suspension.

Aerosol contains: 0,0008-0,1% of usnic acid sodium salt and 0,001-0,1% of essential oil: sage, or thyme, or fennel, or peppermint; or menthol. The procedure starts when in a certain quantity of etanol, usnic acid sodium salt and essential oil: sage, that is thyme, that is fennel, that is peppermint; that is menthol. A certain quantuty of water is added, as well as a certain quantity of glycerine and colour solution. To the ethanolic

solution of usnic acid sodium salt and essential oil, or menthol, the aqueous solution of glycerine and colour is added. To this solution, pressure gas is added.

The invention also presents the procedure for obtaining of pharmaceutical disinfective preparation in the form of **aromatic-antiseptic liquid for disinfection**, which is, according to its content, alcoholic aqueous solution of active antiseptic components, sweetener, colours, and different sabilizers. It is applied as a ready liquid for application without diluting.

Aromatic-antiseptic liquid for disinfection contains: 0,01-0,15% of usnic acid sodium salt and 0,001-0,1% of essential oils: sage, or thyme, or fennel, or peppermint; or menthol. The process starts when in a certain quantity of water, weighed in the vessel for preparation, usnic acid sodium salt is dissolved with stirring. Into this solution, a certain quantity of glycerine and colour solution are weighed. Into weighed quantity of ethanol, the essential oil of sage, or thyme, or fennel, or peppermint; or menthol, is dissolved. This solution is added to the previously prepared one with stirring.

Applicability of the preparation is confirmed by determination of its microbiological activity to the following microorganisms:

Table 2. Microbiological activity of the preparation to *Bacillus subtilis*

<i>Bacillus subtilis</i>	
concentration (mg/cm ³)	zone diameter (mm x 10)
0,0123	160
0,025	195
0,050	215
0,1	275
solvent	0

Table 3. Microbiological activity of the preparation to *Micrococcus pyogenes*

<i>Micrococcus pyogenes</i>	
concentration (mg/cm ³)	zone diameter (mm x 10)

0,0123	160
0,025	175
0,050	205
0,1	225
solvent	0

Table 4. Microbiological activity of the preparation to *Staphylococcus aureus*

<i>Staphylococcus aureus</i>	
concentration (mg/cm ³)	zone diameter (mm x 10)
0,0123	150
0,025	205
0,050	215
0,1	250
solvent	0

Table 5. Microbiological activity of the preparation to *Escherichia coli*

<i>Escherichia coli</i>	
concentration (mg/cm ³)	zone diameter (mm x 10)
0,0123	109
0,025	183
0,050	213
0,1	248
solvent	0

Table 6. Microbiological activity of the preparation to *Candida albicans*

<i>Candida albicans</i>	
concentration (mg/cm ³)	zone diameter (mm x 10)
0,0123	185
0,025	215
0,050	285

0,1	300
solvent	0

Table 7. Microbiological activity of the preparation to *Micrococcus flavus*

<i>Micrococcus flavus</i>	
concentration (mg/cm ³)	zone diameter (mm x 10)
0,0123	109
0,025	083
0,050	213
0,1	248
solvent	0

The enclosed tables show that the preparation has an antibacterial effect at very low concentrations on the following microorganisms: *Bacillus subtilis*, *Micrococcus pyogenes*, *Micrococcus flavus*, *Echerichia coli*, *Staphylococcus aureus* and *Candida albicans*.

Following examples further illustrate, but not restrict the invention.

Example 1. Weigh 75% of glucose in the vessel for granulation. Separately prepare solution of granulation agent weighing 5% of water and heat it to 65°C, adding 0,009% of usnic acid sodium salt, subsequently adding 0,017% of colour and 23% of binder. The solution prepared in such way is used to carry out granulation of glucose, dispersing the solution. When introducing of the solution is finished, the granulate is dried to humidity of 27%. Equalization of the granulate is carried out by screening through 1 mm mesh. To the granulate, 0,05% ethanolic solution of the fennel essential oil is added, introducing by the sprayer. The granulate is dried to the humidity which enables good tableting (max. 22%). The dried granulate is transferred to the vessel for homogenization and 2% of sliding agent is added, the mixture is transferred to the tableting machine, and chewable tablets of weight up to 1200mg are formed.

Example 2. The procedure according to this example goes on like the procedure from example 1, the difference between these two examples is that 0,15% of the fennel essential oil is taken. The other characteristics of the procedure are the same as those from the procedure stated in example 1.

Example 3. Weigh 75,7% of glucose into the vessel for granulation. Separately prepare the solution of granulation agent weighing 4% of water and heat it to 55°C, adding 0,02% of usnic acid sodium salt, 0,007% of colour and 22,3% of binder. The solution prepared in such way is used to carry out granulation of glucose, dispersing the solution. When introducing of the solution is finished, the granulate is dried to humidity of 24%. Equalization of the granulate is carried out by screening through 0,5 mm mesh. To the granulate, 0,2% ethanolic solution of the sage essential oil is added, introducing by the sprayer. The granulate is dried to the humidity which enables good tableting (max. 22%). The dried granulate is transferred to the vessel for homogenization and 2% of sliding agent is added, the mixture is transferred to the tableting machine, and chewable tablets of weight up to 1200mg are formed.

Example 4. The procedure according to this example goes on like the procedure from example 1, the difference between these two examples is that 0,03% of the sage essential oil is taken. The other characteristics of the procedure are the same as those from the procedure stated in example 3.

Example 5. Weigh 74% of glucose into the vessel for granulation. Separately prepare the solution of granulation agent weighing 5% of water and heat it to 75°C, adding 0,01% of usnic acid sodium salt, 0,01% of colour and 20% of binder. The solution prepared in such way is used to carry out granulation of glucose, dispersing the solution. When introducing of the solution is finished, the granulate is dried to humidity of 27%. Equalization of the granulate is carried out by screening through 0,5 mm mesh. To the granulate, 0,005% ethanolic solution of the thyme essential oil is added, introducing by the sprayer. The granulate is dried to the humidity which enables good tableting (max. 22%). The dried granulate is transferred to the vessel for homogenization and 6% of

sliding agent is added, the mixture is transferred to the tableting machine, and chewable tablets of weight up to 1200mg are formed.

Example 6. The procedure according to this example goes on like the procedure from example 1, the difference between these two examples is that 0,17% of the thyme essential oil is taken. The other characteristics of the procedure are the same as those from the procedure stated in example 4.

Example 7. Weigh 75,5% of glucose into the vessel for granulation. Separately prepare the solution of granulation agent weighing 5% of water and heat it to 60°C, adding 0,015% of usnic acid sodium salt, 0,005% of colour and 23% of binder. The solution prepared in such way is used to carry out granulation of glucose, dispersing the solution. When introducing of the solution is finished, the granulate is dried to humidity of 18%. Equalization of the granulate is carried out by screening through 2 mm mesh. To the granulate, 0,08% ethanolic solution of the **peppermint** essential oil is added, introducing by the sprayer. The granulate is dried to the humidity which enables good tableting (max. 22%). The dried granulate is transferred to the vessel for homogenization and 1,5% of sliding agent is added, the mixture is transferred to the tableting machine, and chewable tablets of weight up to 1200mg are formed.

Example 8. The procedure according to this example goes on like the procedure from example 1, the difference between these two examples is that 0,07% of the peppermint essential oil is taken. The other characteristics of the procedure are the same as those from the procedure stated in example 7.

Example 9. Weigh 96,7% of glucose into the vessel for granulation. Separately prepare the solution of granulation agent weighing 5% of water and heat it to 60°C, adding 0,015% of usnic acid sodium salt, 0,00587% of colour and 1,73% of binder. The solution prepared in such way is used to carry out granulation of glucose, dispersing the solution. When introducing of the solution is finished, the granulate is dried to humidity of 18%. Equalization of the granulate is carried out by screening through 2 mm mesh. The

granulate is dried to the humidity which enables good tableting (max. 22%). The dried granulate is transferred to the vessel for homogenization and 1,5% of sliding agent and 0,05% of menthol is added. The prepared granulate is transferred to the tableting machine, and chewable tablets of weight up to 1200mg are formed.

Example 10. Gel with usnic acid sodium salt and essential oils or menthol

Weigh 80,66% of water in the vessel of the apparatus for preparation, add 0,04% of usnic acid sodium salt and stir to dissolving. Subsequently add 1,0% of carboxypolymethylene, stir to homogenization (approximately 15 minutes) and leave to become swollen, for 12 hours. To the gel base, 0,6% sodium hydroxid solution is added slowly, with stirring. Weigh 7,0% of ethanol, dissolve 0,2% solution of sage, or thyme, or fennel, or peppermint essential oil, or menthol. This solution is gradually, with stirring added to the gel-mass to homogenization. After that, a certain quantity of colour solution is added.

Example 11. Aromatic-antiseptic liquid for mouth with usnic acid sodium salt and essential oils or menthol

Weigh 83,96% of water in the vessel for preparation, and 0,03% of usnic acid sodium salt is dissolved with stirring. To this solution, 5% of glycerine and 1% of colour solution are weighed. Into 10% of ethanol, 0,01% solution of the essential oil of sage, or thyme, or fennel, or peppermint; or menthol, is dissolved. This solution is added to the previously prepared one with stirring.

Example 12. Aerosol for mouth with usnic acid sodium salt and essential oils or menthol

Weigh 3,5% of ethanol, and dissolve 0,0187% of usnic acid sodium salt and 0,075% solution of essential oil: sage, that is thyme, that is fennel, that is peppermint; that is menthol. Weigh 84,815% of water, add 7,00% of glycerine and 0,5% of colour solution. To the ethanolic solution of usnic acid sodium salt and essential oil, or menthol, the aqueous solution of glycerine and colour is added and stirred. To this solution, 50% of pressure gas, tetrafluordichlor ethan is added.

PATENT CLAIMS

1. A pharmaceutical disinfective preparation on the basis of medical plants, marked by the characteristic that it contains usnic acid sodium salt in range 0,001% to 0,150% and sage *Salvia officinalis* L. essential oil in range 0,001% to 0,400% and usual pharmaceutical additives in order to obtain suitable pharmaceutical form.
2. A pharmaceutical disinfective preparation according to the patent claim 1, marked by the characteristic that it contains usnic acid sodium salt in range 0,001% to 0,150% and fennel *Foeniculum vulgare* L. essential oil in range 0,001% to 0,400% and usual pharmaceutical additives in order to obtain suitable pharmaceutical form.
3. A pharmaceutical disinfective preparation according to the patent claim 1, marked by the characteristic that it contains usnic acid sodium salt in range 0,001% to 0,150% and thyme *Thymus Vulgaris* L. essential oil in range 0,001% to 0,400% and usual pharmaceutical additives in order to obtain suitable pharmaceutical form.
4. A pharmaceutical disinfective preparation according to the patent claim 1, marked by the characteristic that it contains usnic acid sodium salt in range 0,001% to 0,150% and peppermint *Mentha piperita* L. essential oil in range 0,001% to 0,400% and usual pharmaceutical additives in order to obtain suitable pharmaceutical form.
5. A variant solution of the preparation according to the patent claim 1, marked by the characteristic that it contains usnic acid sodium salt in range 0,001% to 0,020% and menthol in range 0,05% to 0,1% and usual pharmaceutical additives in order to obtain suitable pharmaceutical form.
6. A procedure for obtaining of **chewable tablets** with usnic acid sodium salt and essential oil: sage, or fennel, or thyme, or peppermint, or menthol, marked by the fact that a certain quantity of glucose is weighed, a granulation agent solution is prepared separately, and usnic acid sodium salt is added, the solution prepared in such manner

is used to carry out granulation of glucose by dispersing the solution, the granulate is dried to humidity in range 5% to 30%, and to the cooled granulate, the essential oil ethanolic solution of: fennel, or sage, or thyme, or peppermint, or menthol is added, using sprayer, the granulate is dried to humidity max. 22%, to the dried granulate a certain quantity of sliding agent is added in the vessel for homogenization, and the granulate is converted to the corresponding suitable pharmaceutical form.

7. A procedure for obtaining of **chewable tablets** with usnic acid sodium salt and essential oil: sage, or fennel, or thyme, or peppermint, or menthol, marked by the fact that usnic acid sodium salt is dissolved in water, a certain quantity of carboxypolymethylene is added, the mixture is stirred to homogenization and left to become swollen for 7-21 hours, and then, a neutralizing agent, such as sodium hydroxid solution, is added slowly, with stirring, and subsequently, to the gel-mass the essential oil ethanolic solution of fennel, or sage, or thyme, or peppermint, or menthol is added with stirring to homogenization, and finally, the colour solution is added.
8. A procedure for obtaining of **aerosol** with usnic acid sodium salt and essential oil: fennel, or sage, or thyme, or peppermint, or menthol, marked by the fact that in a certain quantity of ethanol usnic acid sodium salt is dissolved, as well as the essential oil of sage, or thyme, or fennel, or peppermint; or menthol, a certain quantity of water is added, a certain quantity of glycerine and colour solution are added as well, and to the prepared solution, pressure gas is added.
9. A procedure for obtaining of **aromatic-antiseptic liquid for disinfection** with usnic acid sodium salt and essential oil: fennel, or sage, or thyme, or peppermint, or menthol, marked by the fact that in a certain quantity of water usnic acid sodium salt is dissolved with stirring, a certain quantity of glycerine and colour solution is weighed, the essential oil ethanolic solution of: sage, or thyme, or fennel, or peppermint; or menthol is added with stirring to the previously prepared solution.

10. An application of usnic acid sodium salt in combination with the essential oil: fennel, or sage, or thyme, or peppermint, or menthol, according to the patent claims 1 to 5, for obtaining of pharmaceutical and cosmetic preparations for disinfection and external application.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/YU 00/00022

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/343 A61K35/78 A61P31/02 //(A61K35/78, A61K31:34)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, EMBASE, BIOSIS, SCISEARCH, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 256 566 A (ISCOFAR SAS) 24 February 1988 (1988-02-24) page 6, line 5 - line 6; example 1	1-10
X	WO 00 03612 A (SCHUER JOERG PETER) 27 January 2000 (2000-01-27) page 11, line 11 - line 15; claims 5,7	1-10
X	DE 23 54 517 A (HANDELSGESELLSCHAFT SCHLOSSER) 28 May 1975 (1975-05-28) page 1, line 2 - line 3; examples 1,2 -/-	1-10

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE WPI Section Ch, Week 198942 Derwent Publications Ltd., London, GB; Class B04, AN 1989-307066 XP002164530 & RO 96 751 A (INST CERC CHIMICO-FARM), 28 April 1989 (1989-04-28) abstract</p>	1-10
X	<p>FR 2 662 939 A (BEAUSSIER YANN) 13 December 1991 (1991-12-13) page 1, line 11 - line 12 page 1, line 28 - line 33 page 3, line 3 - line 6</p>	1-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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